REMARKS

I. Status of claims

Claim 1, and 6 are amended.

Claim 2 is cancelled.

Claims 3-5, 7-35 and 37 are withdrawn.

Claims 1, 6, and 36 are pending.

II. Claims 1, 6 and 36 satisfy §112 2nd paragraph requirements

The examiner rejected claims 1, 6, and 36 under §112 second paragraph requirements. Claims 1 and 6 are amended. Support can be found throughout the specification, especially in paragraphs [00149-153] of the specification as filed and the accompanying figures.

Gadd45β-binding region(s) of MKK7/JNKK2 were mapped using sets of N- and C-terminally truncated MKK7 polypeptides (see FIG. 29a and FIG. 29c, respectively). The specification as filed provides sufficient written description as to the various domains/regions of JNKK2 that were mapped for interaction with Gadd45β. Mutations occurring between amino acids 157 and 213 in JNKK2, interacted weakly with GST-Gadd45β (see FIG. 29b). It was demonstrated that JNKK2 contacts Gadd45β through two distinct regions. The specification also demonstrates that the two domains are located within the kinase domain of KNKK2 (paragraph 00149).

Claim 1 is amended to indicate that the peptide, by disrupting the Gadd45β-mediated suppression of JNKK2 activation, is able to promote programmed cell death. The specification describes the functional relationships between Gadd45β-JNKK2 interaction. One of skill in the art would understand the steps needed to increase JNK activation according to claim 1 in light of the specification. If the examiner doubts this, he needs to explain what other steps are needed.

III. Claims 1 and 6 satisfy §112 written description and enablement requirements

On page 4 of the Action, the examiner rejected claims 1 and 6 under §112 first paragraph written description and enablement requirements. The claims are to **methods** not products, or compounds so the case law cited by the examiner is not on point. The specification, as filed discloses several peptides derived from JNKK2 that interact with Gadd45β to enable a skilled artisan to practice the claimed methods. The specification provides sufficient guidance for the peptide genus. A detailed mapping analysis of the JNKK2-Gadd45β interaction provides sufficient specifics for a genus comprising JNKK2-derived peptides.

The specification provides guidance for skilled artisan to design cell permeable, fusion peptides encompassing the amino acid regions of JNKK2 that come into direct contact with Gadd45β (paragraph 00113 of the specification). These peptides effectively compete with endogenous Gadd45β proteins for binding to JNKK2, as evidence by the Peptide 1 (FIG. 30 and Example 12).

The specification as filed provides a working example of a fusion peptide with a specific sequence structure. For example, the specification discloses that a peptide comprising a sequence of GPVWKMRFRKTGHVIAVKQMRRSGN functions a specific blocking peptide that blocks Gadd45β inactivation of JNK pathway. This sequence has a specific structure (the peptide sequence) and this structure is correlated with a specific function, i.e., blocking Gadd45β interaction with JNKK2. The law does not require every conceivable embodiment to be tested and validated. *See e.g., See Engle Indus., Inc. v. Lockformer Co.*, 946 F.2d 1528 (Fed. Cir. 1991); *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524 (Fed. Cir. 1987). The inventors of the present application discovered a novel mechanism of inhibition of JNK pathway by Gadd45β and this inventive concept is intended to be covered by the claims. The fusion peptide is just one such method of inhibiting Gadd45β and JNKK2 interaction.

The examiner has not provided any evidence to dispute applicants representation that the *in vitro* data provides adequate correlation to the *in vivo* effects. However, the examiner simply argues that the *in vitro* data does not predict that the invention would function as claimed (page 12 of the Action).

The effects claimed are blocking suppression of activation of JNK thereby leading to increased cell death. The *in vitro* models used are standard and have been shown to reasonably correlate to *in vivo* effects. Apoptosis is the active participation of the cell in its own destruction through the execution of an intrinsic suicide program. Some of the factors in apoptosis have been studies by those of skill in the art using knock-out models, such as that used in the inventors' declaration of record.

Showing that Gadd45ß binds to and inhibits JNKK2 *in vitro*, thereby removing a barrier to apoptosis, coupled with the evidence that absence of Gadd 45ß *in vivo* removes a barrier to apoptosis, is sufficient to support the pending claims.

Given that the claims are to methods of JNK activation, the full-length sequence of JNKK2 is known and as disclosed in the specification, based on the data and guidance in the specification (e.g., various interaction domains, mapping analysis, and exemplary demonstration with Peptide 1 fusion protein), a skilled artisan is enabled to practice the method claims without undue experimentation.

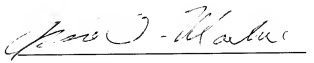
Applicant's maintains the argument that the examiner has no legal support to extrapolate from the end points of the method claims, programmed cell death, to treatment of "all diseases." All that is required for written description and enablement is that the claimed method increases programmed cell death and that has been shown. It is not necessary to prove all diseases benefit from application of the method. Although use of the claimed method may lead to disease treatment, whether successful or not, the claims herein are operative if programmed cell death is increased. *In vitro* use to increase programmed cell death is possible, so it is predictable that cells would also die *in vivo*.

IV. Other Issues

If pending claims are allowable, and a terminal disclaimer over U.S. Serial No. 10/263,330 is necessary, it will be filed. If there are still issues, an interview is also requested.

No other fees are believed due at this time, however, please charge any deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21416-94575).

Respectfully submitted,



Alice O. Martin
Reg. No. 35,601

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BARNES & THORNBURG LLP
P.O. Box 2786
Chicago, Illinois 60690-2786
(312) 357-1313

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